

IB. AMENDMENTS TO THE CLAIMS

Please enter the amendments to claims 1, 23, 28, and 31, as shown below.

Please enter new claims 32-38, as shown below.

1. (Currently amended) A method of inhibiting formation of neurofibrillary tangles in an individual, said method comprising: administering to the individual an agent that reduces ~~reducing~~ formation of a neurotoxic carboxyl-terminal truncated form of apoE in a neuron in the individual, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, and wherein formation of neurofibrillary tangles is inhibited.

2. (Original) The method of claim 1, comprising administering to the individual an agent that reduces a proteolytic activity of an enzyme that catalyzes the proteolytic degradation of apoE in a neuronal cell.

al 3. (Original) The method of claim 1, wherein the reduction in formation of carboxyl-terminal truncated apoE treats a disorder related to apoE in an individual.

4. (Original) The method of claim 3, wherein the disorder is selected from the group consisting of Alzheimer's disease, coronary artery disease, head trauma, and stroke.

5. (Original) The method of claim 3, wherein the apoE is apoE4.

6. (Original) The method of claim 5, wherein the carboxyl-terminal truncated form of apoE4 is apoE4 (Δ 272-299).

7.-22 (Withdrawn)

al 23. (Currently Amended) A method of inhibiting formation of neurofibrillary tangles in a neuronal cell of an individual, the method comprising: contacting the neuronal cell with an agent that inhibits an enzymatic activity of an enzyme in the neuronal cell that catalyzes cleavage of apoE in the

cell to generate neurotoxic carboxyl-terminal truncated apoE, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE.

a¹ 24. (Original) The method of claim 23, wherein the agent is a peptide selected from the group consisting of Ala-Ala-Pro-Phe (SEQ ID NO:1), Ala-Ala-Pro-Leu (SEQ ID NO:3), and Ala-Ala-Ala-Ala-Pro-Phe (SEQ ID NO:4).

25.-27. (Withdrawn)

a¹ 28. (Currently Amended) A method of treating Alzheimer's disease, the method comprising: administering an inhibitor of a chymotrypsin-like serine protease in an amount effective to inhibit an enzyme that catalyzes the formation of carboxyl-terminal truncated apoE in a neuronal cell, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, and wherein the enzyme is inhibited and the level of neurofibrillary tangles in a neuronal cell in the individual is reduced.

29.-30. (Withdrawn)

31. (Currently Amended) A method of reducing the level of carboxyl-terminal truncated apoE in a neuronal cell, the method comprising:

a¹ contacting the cell with an agent that reduces activation of an enzyme that catalyzes the formation of neurotoxic carboxyl-terminal truncated apoE in a neuronal cell, wherein said enzyme is activated by A β ₁₋₄₂, wherein a reduction in the activation of the enzyme results in a reduction in the level of neurotoxic carboxyl-terminal truncated apoE in the cell.

-- 32. (New) A method of reducing formation of neurotoxic carboxyl-terminal truncated apoE in a neuronal cell in an individual, the method comprising contacting the cell with an agent that reduces formation of carboxyl-terminal truncated apoE in the individual, wherein the carboxyl-terminal truncated apoE comprises amino acids 244-260 of apoE, and wherein formation of neurotoxic carboxyl-terminal truncated apoE in the cell is reduced.

33. (New) The method of claim 1, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD.

34. (New) The method of claim 1, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD.

35. (New) The method of claim 23, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD.

36. (New) The method of claim 23, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD.

a 37. (New) The method of claim 32, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 28 kD to about 30 kD.

38. (New) The method of claim 32, wherein the carboxyl-terminal truncated form of apoE has a molecular weight of from about 14 kD to about 20 kD. --
